

AMENDMENTS

IN THE DRAWING

Please replace original drawing sheets 1-12 (13 pages) with formal drawing sheets 1-12 (13 pages) submitted herewith.

IN THE CLAIMS

Claims 1-20 (cancelled).

21. (Currently Amended) An isolated polynucleotide for enhancing protein expression, wherein said polynucleotide comprising comprises a nucleic acid sequence of nucleotides 181-341 of SEQ ID NO: 1 having one thymidine inserted between position 206 and 207 of SEQ ID NO: 1, or a fragment thereof that includes said thymidine, wherein said the polynucleotide or the fragment enhances protein expression when incorporated downstream of an expression regulatory promoter sequence and upstream of a protein coding sequence.

22. (Currently Amended) The isolated polynucleotide according to claim 21, wherein said nucleic acid sequence has translation promoting activity to enhance expression of a nucleic acid sequence encoding a protein sequence. enhances said protein expression by increasing translation of the mRNA encoding said protein.

23. (Currently Amended) The isolated polynucleotide according to claim 21, wherein said nucleic acid sequence enhances said protein expression by increasing IRES activity.

24. (Currently Amended) An isolated polynucleotide that enhances for enhancing protein expression, which included wherein the polynucleotide comprises a nucleic acid sequence set out in SEQ ID NO: 7 and enhances protein expression by promoting mRNA translation in an IRES dependent manner when incorporated 5' of a protein coding sequence in an expression construct by promoting mRNA translation in an IRES dependent manner, said polynucleotide comprising a nucleotide sequence of SEQ ID NO: 7.

Claim 25 (cancelled).

26. (Previously Amended) An isolated polynucleotide consisting of the nucleotide sequence as set forth in SEQ ID NO: 7 over its entire length.

Claim 27 (cancelled).

28. (Previously Amended) An expression vector comprising an isolated polynucleotide according to claim 21 or claim 24.

29. (Currently Amended) A An isolated host cell transformed or transfected with the vector according to claim 28.

30. (Currently Amended) A method of expressing a protein *in vitro*, comprising the steps of:

(a) transforming or transfecting a an isolated host cell with an the expression vector according to claim 53, and

(b) growing the host cell in a medium under conditions where the cell expresses the protein.

31. (Currently Amended) A The method according to claim 30, wherein the method further comprising comprises, after step (b), a step of isolating the protein from the cell and/or the growth medium.

Claim 32 (cancelled).

33. (Previously Amended) A probe for screening substances that interact with IRES, comprising the polynucleotide according to claim 26, further comprising a detectable label.

34. (Previously Amended) A probe for screening IRES-dependent translation inhibitors, comprising the polynucleotide according to claim 26, further comprising a detectable label.

35. (Previously Amended) A composition comprising the isolated polynucleotide for enhancing protein expression according to claim 21.

36. (Previously Amended) A composition comprising the isolated polynucleotide for enhancing protein expression according to claim 24.

37. (Previously Amended) A method for determining a hypervirulent hepatitis C strain, comprising the steps of:

(a) screening a biological sample for the presence of the polynucleotide according to claim 26, and;

(b) determining presence or absence of the hypervirulent hepatitis C strain from the screening step, wherein the presence of the polynucleotide identifies the hypervirulent hepatitis C strain in the biological sample and the absence of said sequence indicates the absence of said hypervirulent hepatitis C.

38. (Previously Amended) An isolated polynucleotide according to claim 21, further comprising nucleotides 1-180 of SEQ ID NO: 1.

39. (Previously Amended) An isolated polynucleotide according to claim 21 or 38, further comprising nucleotides 342-713 of SEQ ID NO: 1.

Claims 40-43 (cancelled).

44. (Currently Amended) An The isolated polynucleotide according to
claim 21 or 24 comprising a nucleic acid sequence for enhancing protein expression
according to claim 24, wherein the a 5'-untranslated region comprising of the nucleic acid
sequence comprises a polynucleotide sequence corresponding to at least one region selected
from the group consisting of pyrimidine-rich tract, Box A, Box B, a trans factor-binding site,
and a combination thereof.

45. (Currently Amended) An isolated polynucleotide comprising a nucleic
acid sequence for enhancing expression of a nucleic acid sequence according to claim 24 for
enhancing protein expression, wherein said polynucleotide comprises a nucleotide sequence
of SEQ ID NO: 7, nucleotides 181-341 of SEQ ID NO: 1 having one thymidine inserted
between position 206 and 207 of SEQ ID NO: 1 or a fragment thereof that includes said
thymidine, and wherein said nucleic acid comprises a sequence has a substitution, deletion,
insertion, and/or addition of a single or a few nucleotide nucleotides of a sequence derived
taken from a gene of wild type virus within the sequence or proximate sequence in at least
one position corresponding to a pyrimidine-rich tract, Box A, Box B, and/or trans factor-
binding site contained in the 5'-untranslated region said nucleic acid sequence.

Claims 46 (cancelled).

47. (Currently Amended) The isolated polynucleotide according to claim 24 44, wherein the 5'-untranslated region comprises at least one pyrimidine-rich tract

48. (Currently Amended) The isolated polynucleotide according to claim 24 44, wherein the 5'-untranslated region comprises a sequence corresponding to a region selected from the group consisting of Box A, Box B, a trans-binding site, and a combination thereof.

49. (Currently Amended) The isolated polynucleotide according to claim 24 44, wherein the 5'-untranslated region comprises an AUG or ATG sequence.

50. (Currently Amended) The isolated polynucleotide according to claim 24 44, wherein the 5'-untranslated region comprises a part or an entire region of IRES of viral mRNA.

51. (Currently Amended) The isolated polynucleotide according to claim 24 44, wherein said nucleic acid sequence further comprises a portion of a coding region taken from a viral gene adjacent to the 5'-untranslated region.

52. (Previously added) The isolated polynucleotide according to claim 24, wherein said nucleic acid is a cDNA sequence.

53. (Previously added) An expression vector according to claim 28, further comprising a protein coding sequence operably inserted downstream of the polynucleotide for enhancing protein expression.

54. (Previously added) An isolated polynucleotide comprising nucleotide 181-341 of SEQ ID NO:1, wherein said polynucleotide includes a thymidine inserted between position 206 and 207 of SEQ ID NO:1.

55. (Previously Added) An expression vector comprising a promoter sequence, a polypeptide encoding sequence, and a nucleic acid sequence of SEQ ID NO: 7 incorporated downstream of the promoter sequence and upstream of the polynucleotide encoding sequence, wherein the nucleic acid sequence of SEQ ID NO: 7 enhances expression of the polypeptide by means of increasing IRES activity.

56. (Currently Amended) The expression vector according to claim 55, wherein said gene expression vector is a vector for expression in eukaryotic cells.

57. (New) An isolated polynucleotide for enhancing protein expression, wherein said polynucleotide comprises the nucleic acid sequence of SEQ ID NO: 7, or a fragment thereof, wherein the polynucleotide or the fragment enhances protein expression by promoting mRNA translation in an IRES independent manner.

58. (New) The isolated polynucleotide according to claim 57, wherein said nucleic acid sequence comprises at least one region selected from the group consisting of pyrimidine-rich tract, Box A, Box B, a trans factor-binding site, and a combination thereof.

59. (New) The isolated polynucleotide according to claim 58, wherein said nucleic acid sequence comprises at least one pyrimidine-rich tract.

60. (New) The isolated polynucleotide according to claim 58, wherein said nucleic acid sequence comprises a sequence corresponding to a region selected from the group consisting of Box A, Box B, a trans-binding site, and a combination thereof.

61. (New) The isolated polynucleotide according to claim 58, wherein said nucleic acid sequence comprises an AUG or ATG sequence.

62. (New) The isolated polynucleotide according to claim 58 wherein said nucleic acid sequence comprises a part or an entire region of IRES of viral mRNA.

63. (New) The isolated polynucleotide according to claim 58, wherein said nucleic acid sequence further comprises a portion of a coding region taken from a viral gene adjacent to said nucleic acid sequence.

64. (New) An expression vector comprising the isolated polynucleotide according to claim 57.

65. (New) A composition comprising the isolated polynucleotide according to claim 57 which enhances protein expression.